

# Review of: "Predictors of Radiation-induced Hypothyroidism in Nasopharyngeal Carcinoma Survivors after Intensity-modulated Radiotherapy"

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**Potential competing interests:** The author(s) declared that no potential competing interests exist.

1. This study investigates the long-term rate and risk factors of radiotherapy-related primary or central hypothyroidism in NPC patients after IMRT, and relevant dose-volume constraints. The goals are of clinical significance and the manuscript is well written. The inclusion of both primary and central hypothyroidism gives the study a higher value.
2. The study was an update of a previously published research (reference 18). Therefore, a sentence or two showing the necessity of an update is helpful for the readers to know what is new in the updated version.
3. Following the above comment, the authors say the previous report is an interim analysis. This makes me wonder what the nature of this study is. It seems to me it is a retrospective, cross sectional observational cohort study. If so, there should not be an interim analysis. Please clarify the study design.
4. One thing that I would like to learn is that how many of the hypothyroidism patients are having subclinical and how many are clinical disease. This piece of information is both of clinical interest and of research impact. Subclinical hypothyroidism is a common diagnosis and the reported prevalence was 3.1% in Korea, 4.3% in the USA (Endocrinol Metab 2021 Jun;36(3):500-513), and up to 20% depending on country, sex, age and the reference range for the diagnosis (Cooper DS, et al. Lancet 2012;379:1142-54). The division of clinical and subclinical will clarify the risk of hypothyroidism that needs treatment.
5. Relevant to the above comment, there were 5% of patients who had thyroid surgery or abnormal TSH levels and were excluded. The percentage of patients excluded due to abnormal TSH level without thyroid surgery is worth mentioning.
6. A review of existing studies on radiotherapy-related hypothyroidism specifically in NPC patients, which are many, would make the manuscript even more informative.
7. Treatment planning should reveal more details of radiotherapy technique including linear accelerator brand name. Whether adjuvant chemotherapy was used should also be stated. The commonly used chemotherapy regimens may also be added.
8. The use of PTV-CTV1, PTV-CTV2 is inconsistent with ICRU reports. According to ICRU Report 62, 78 and 83, the namings for prescribing and reporting IMRT dose include only GTV, CTV, ITV and PTV, with

additional extensions like PTVnd or PTV1, etc.. Therefore, the PTV-CTV1 is not in line with the international naming conventions and may cause confusion.

9. Relevant to the above comment, the use of Dpmean, Dtmean, Vt30, etc., is also confusing. There is only Dmean, V30 and so on. The reader will always understand V30 of thyroid, while Vt30 may cause confusion.
10. "Radiation physician" seems an unusual usage, why not "radiation oncologist"?